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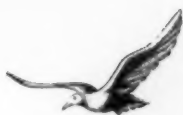
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E D I T O R I A L

PROFESSIONAL ETHICS OR PERSONAL GAIN?

PHARMACISTS have been quite outspoken against the operation of physician-owned pharmacies and it would indeed be a threat to the private practice of pharmacy should this unethical and unfair competition continue to grow. Not only have resolutions been passed by many pharmaceutical organizations condemning this invasion of pharmacy by the medical profession but organized medicine itself has gone on record opposing it.

It is probably not the prerogative of pharmacy to criticize the medical profession and it is true that we have much to do to put our own house in order. However, we still find it difficult not to call attention to certain actions which are contrary to both professional ethics and to the public interest. Recently our attention was drawn to a new development in certain areas and one which seems to be unhealthy and not a credit to the physicians involved. It seems that several physicians will band together and start a small manufacturing business, or possibly we should say a packaging business. A poly-vitamin capsule, among other things, is a favorite item. Products are given a trick proprietary name and are listed at an even trickier price. From now on every patient for whom these products conceivably may be prescribed gets a prescription for them. For example, no matter what the diagnosis a prescription for the polyvitamin product is given along with whatever other therapy may be needed. The vitamins do no harm and it means an extra dollar or so return from the company in which the physician has an interest.

It is difficult to understand how a physician, pledged to consider his patient's welfare above all else, can be guilty of such a practice but we suppose the human frailty of greed is not unknown to certain physicians as well as to pharmacists. The splitting of fees is a similar unethical practice and this we fear is done not only between some physicians but between some physicians and pharmacists. Pharmacists guilty of this or of the pernicious practice of coded prescriptions deserve nothing but condemnation.

Strictly speaking, physicians have a legal right to invest their money wherever they please but it seems doubtful whether this can be done in any area of pharmacy without undue influence on their prescribing habits. It is hazardous for a physician to place himself in the position where public welfare is likely to be jeopardized by personal gain. Keeping the cost of medical care as low as is compatible with good medical care is the duty of every physician as well as every pharmacist. Unless we assume the responsibility for doing this we may yet lose the advantages of free enterprise and be engulfed by state medicine which we have reason to both fear and detest.

We believe that most physicians, just as most pharmacists, are motivated by a sincere regard for the public welfare. We must, however, constantly guard our professions against serious derelictions even on the part of a few. Quite like the world situation today, complacency on the part of many makes it possible for a few evil men to disrupt society and the world. The same is true in our professions; if the few who are unethical go unchallenged they may well destroy our prestige and bring about a public clamor that may shake us to the very roots of our profession.

The medical profession, in particular, these days is faced with powerful and cunning enemies. The independence of medicine stands as a road-block to those who would regulate and control all avenues of our life. Let us not provide our enemies with ammunition with which to harm us.

A high standard of professional conduct and a sincere regard for public welfare are just as essential in our fight to maintain our independence as is a direct and frontal attack on our enemies, their motives and their social philosophy.

In a democracy, if it is to work, it is essential that each individual feel a responsibility not only for his own actions but feel duty bound to take the necessary steps to develop a sense of responsibility in those who lack it. This we must all do in our contacts with our fellow members of the health professions. We cannot enjoy the fruits of democracy and independence without making some personal sacrifices in its behalf.

L. F. TICE

IN VITRO STUDIES RELEVANT TO CONTROL OF SECONDARY RESERVOIRS OF RESPIRATORY PATHOGENS *

By Emil G. Klarmann, Eleanore S. Wright
and Vladimir A. Shternov **

Introductory Remarks

RESPIRATORY diseases, like those of the digestive organs, can be spread either directly by contact, or indirectly via the aerial route which serves as the vector of the suspended infectious particles. In connection with the latter, the following modes of transmission must be considered:

(1) droplet infection, implying direct impingement of the ejected infective matter upon, e. g., the mouth, the conjunctiva, the open wound, etc.,

(2) infection by droplet nuclei, implying inhalation of the minute residues of evaporation from droplets which because of their smallness and lightness may remain suspended in the air for long periods of time,

(3) infection by contaminated dust representing a "secondary reservoir" of infective particles which accumulate on the floors, also on clothes, blankets, etc., and which may become suspended in the air for comparatively short periods of time, particularly following some mechanical activity, such as sweeping.

Recent work at the Columbia School of Public Health indicates that about three-fourths of the bacteria which can be recovered from the air are combined with some floating material having a particle size about 5 microns; therefore, only a comparatively small percentage appear to persist as original droplet nuclei (1). These findings are also in agreement with those of DuBuy and collaborators (2). It is to be expected therefore, that the infected floating par-

* Presented, in part, before the American Society of Hospital Pharmacists, Atlantic City, May 2nd, 1950.

** Plant Research Laboratory, Lehn & Fink Products Corporation, Bloomfield, N. J.

ticles of 5 microns or larger eventually will settle to the floor where they will contribute to the reservoir of infection laden dust.

The comparative significance of the three modes of transmission of respiratory infection listed above has been discussed previously, in considerable detail, by Klarmann (3) who also attempted to give a critical review of the several defensive measures directed toward a control of the spread of such air-borne infections. In the present study reference will be made especially to the third mode, viz., that of infection by contaminated dust, in which, moreover, the pathogenic bacteria are likely to be protected by dried mucous discharge. In this connection it should be remembered that the environmental air may serve as the vector of the fomites of respiratory infection, raised from their "secondary reservoirs" by drafts, mechanical activity, etc. This is not the place, however, to discuss the several methods suggested as means of combating the suspended infectious particles with the view to depriving them of their capacity to do harm. Suffice it to say that a tremendous amount of work has been devoted to the treatment of air by such means as germicidal ultra-violet radiation, disinfectant sprays and aerosols, and disinfectant vapors; a review of any one of these procedures, let alone of all of them, would by far exceed the framework of this presentation. At any rate, recent findings tend to show that the success of direct air disinfection is rendered problematical as long as the microbes are associated with dust, or dry mucus, or both, thereby acquiring substantial protection against the antibacterial procedures aiming at the sterilization of the environmental air spaces.

As indicated previously (3), there is no adequate reason to believe that the attempted mechanical fixation of dust particles by oiling is likely to be so effective as to supply the eventual solution of the problem under discussion. Attempts to effect a control by such means have been made both here and abroad; yet it cannot be said that they have been crowned with complete success.

If, as it now appears, the purely mechanical "fixation" of infectious particles in the secondary reservoirs leaves something to be desired, it would seem logical to inquire into the effectiveness of control of this source of infection by means of disinfectants. By way of setting up criteria of practical fitness of such products, one would have to demand first that they be capable of killing resistant strains of microbes, such as streptococci, staphylococci and tubercle bacilli,

not only in broth, but also when dried in mucus, and mixed with dust, lint, etc., and that they render proof of their capacity for effective and prolonged suppression of bacterial activity. (Another requirement, of a psychological rather than a bacteriological character would call for a substantial freedom from odor, since strongly odorous products, such as those of the crude coal tar variety, are likely to become objectionable to the patient or to the hospital staff who would be exposed to their smell continuously over long periods of time.)

Although, particularly in recent times, antibacterial substances have been drawn from different classes of chemicals, the evaluation of their fitness for general disinfecting purposes is still being carried out largely by means of a testing method originally designed for products of a phenolic character. This is not the place to stress the lack of propriety implied in the use of such a method for testing products which are totally different from phenol, both in their chemical character and in their mode of antibacterial behavior.

Much has been said also about the "safety margin" in calculating *use* dilutions from the phenol coefficients of various disinfectants. This "safety margin" depends upon the *presumed* analogy of a given disinfectant concentration to a 5 per cent phenol solution which, as is known, is strongly bactericidal for all vegetative pathogens. The original determination of the phenol coefficient (with the Gram negative *S. typhosa* as test organism) does not consider certain significant factors such as Gram positive bacteria, organic material, dust, etc., present under practical conditions; accordingly it must have been assumed arbitrarily by the proponents of this principle that, indeed, there exists an adequate similarity in the bactericidal performance of the 5 per cent phenol solution on one hand, and of the disinfectant solution under consideration on the other, to warrant the belief that all these factors would be taken care of automatically, and that a sufficiency of bactericidal power will be available to achieve the desired result of disinfection (4).

As to the action of disinfectants upon different bacteria, it has been demonstrated amply and repeatedly that it does not run parallel to that upon *S. typhosa*, and that this divergence is not only characteristic of certain classes of disinfectants (5) but that it is found also among the members of a homologous series within one class (6).

The effect of the various forms of organic matter upon the performance of different bactericides is the subject of numerous investigations whose discussion or review would be beyond the scope of this paper (7).

Experimental Part

With particular reference to the role of dust and dirt as vehicles of infectious microorganisms entering the host *via* the respiratory route, this report deals with a method for testing contaminated surfaces which have been cleaned with a disinfectant solution. An attempt has been made to develop a *use* test, involving conditions which are found in regular practice.

As pointed out in the introduction, infectious bacteria, as found on floors, are most likely to be protected by some sort of mucous discharge. This, in turn, becomes mixed with the dust on the floor. With this in mind, two series of tests were run, one calling for a mixture of culture and saliva, and the other for a mixture of culture, saliva and dust. Cultures of *Strep. hemolyticus*, *M. pyog. aureus* and *M. tuberculosis* were selected for this series of tests as being most representative of the types of bacteria found on floors. Glass slides 3" x 1" were used to represent the contaminated surfaces because they were easy to sterilize and to manipulate in other ways. Such slides, when left on the floor of the laboratory for one week, were found to accumulate 0.3 to 0.6 milligram of dust per slide, depending upon the location in which they were placed. The question of the length of time during which the disinfectant was to act on the contaminated surface was settled by observing actual conditions. It was noted that about 10 minutes elapsed between the time when a section of the laboratory floor was moistened with a mop until the time when it was thoroughly dry.

Preparation of Test Material

The mixtures for inoculating the slides were prepared as follows: Saliva was collected by chewing paraffin. The saliva was then pasteurized by heating in a tightly stoppered bottle, completely submerged in a water bath for 30 minutes at 60 to 65° C. After this treatment, none, one or two colonies per cc. developed upon plating. To 10 cc. of pasteurized saliva was added 1 cc. of culture. In the case of *Strep. hemolyticus* we used a 24 hour broth culture which showed the following resistance to phenol at 20° C.

1:60	—	—	—
1:70	+	+	—
1:80	+	+	+

This strain was much more resistant than some recently isolated strains and was selected for that reason. The strain of *M. aureus* was 209; it was prepared for the test according to the AOAC method and answered the requirements of this method as to phenol resistance (48). The strain of *M. tuberculosis* used was 607; it was selected because it grew well and rapidly on culture media and was more resistant to phenol than two freshly isolated strains tested. The test culture was grown on glycerin broth for 7 days at 37° C. Before using, it was thoroughly mixed with a 10 cc. pipette, allowed to stand for a few minutes, and the amount needed for the test pipetted from the clear zone. The phenol resistance of the test culture at 20° C. was:

1:60 — — —

1:70 + + —

1:80 + + +

If dust was to be used in inoculating the slides the amount needed to make a final dilution of 0.5% was sterilized in the hot air oven for $\frac{1}{2}$ hours at 160 to 170° C. This was two to four times as much dust as had collected on the slides naturally. The dust used in these experiments was collected from a vacuum cleaner bag and passed through a 20 mesh sieve before being used.

Green glass slides 3" x 1" were sterilized in covered trays placed in a hot air oven at 160 to 170° C. for two hours. The tray was also fitted with a cardboard cover which was treated under an ultra-violet light; this cardboard cover was used to permit thorough drying of the slides following inoculation.

Using a 1 cc. pipette, slides were inoculated with five 0.05 cc. drops of the prepared culture mixture. When dust was used in the inoculum, only one slide at a time was inoculated from the pipette, and the inoculum was remixed in the tube before being placed on each slide. The cardboard covers were then placed on the boxes of slides and the slides allowed to dry spontaneously for 18 to 24 hours at 20 to 22° C.

Testing Procedure

The disinfectant solutions were made up in sterile distilled water and kept at 20° C. One cc. was placed on each slide and spread over the slide with a nichrome spreader, care being taken to pull the

spreader along the edges of the slides and not to disturb the formation of the dried drops. At the end of 10 minutes, the slide was carefully picked up and placed in a large tube containing 80 cc. of sterile distilled water. The surface of the slide was then scraped with a rubber scraper (which was kept in boiling water when not in use), mixed thoroughly, and a 1 cc. sample pipetted into a petri dish. If the test was being made with *Strep. hemolyticus* the petri dish contained 2 cc. of sterile citrated horse blood, and 20 cc. of streptococcus agar at 45° C. was then poured into the plate and mixed thoroughly. In the case of *M. pyog. aureus*, 2 cc. of horse serum and 20 cc. of AOAC agar were used. When running the test with *M. tuberculosis* the one cc. was inoculated onto the surface of the agar in the petri dish and the dish tilted to insure an even distribution of the inoculum. *Strep. hemolyticus* and *M. pyog. aureus* plates were incubated for 48 hours at 37° C. *M. tuberculosis* plates were incubated without inverting for two or three days until fairly dry, then inverted and incubated four or five days more, for a total incubation period of seven days. Colony counts were made and the number of bacteria surviving per slide were calculated.

When these tests were first run the slides themselves as well as the 1 cc. sample were plated because it was felt that all bacteria might not have been removed from the slides by scraping. However, the number of bacteria left on the slide made no substantial difference in the final count; therefore, the plating of slides was omitted in subsequent tests.

Care was taken to determine the occurrence or non-occurrence of bacteriostasis in all tests. It was found that benzalkonium chloride (10%) and benzethonium chloride (10%) when diluted with water 1:10, were almost completely bacteriostatic for *M. tuberculosis* under the conditions of the test procedure. This had to be overcome by the following means: When the 1 cc. sample was withdrawn from the tube containing the test slide, it was mixed first with 1 cc. of blood which was found previously to be capable of suppressing the bacteriostatic action of quaternary ammonium compounds (8). After standing for ten minutes, 1 cc. was then inoculated onto the surface of the agar in the petri dish. Controls made in this way showed no growth in the absence of blood; however, growth occurred if blood (or serum) was used as the "neutralizer". (Blood seemed to be more effective than serum.)

The following culture media were employed:

For Streptococcus hemolyticus (Lederle 7):

Broth:

Difco Protesose Peptone No. 4	20	grams
Difco Yeast Extra	3	grams
Dextrose	2	grams
NaCl	5	grams
Dipotassium phosphate	2.5	grams
per liter—pH 7.2 to 7.4		

Agar:

Add 1.5 per cent agar to the above. Before pouring plates add 10 per cent sterile citrated horse blood.
pH 7.2 to 7.4

For M. pyog. aureus:

Broth: Regular AOAC

Agar: AOAC agar plus 10 per cent horse serum

For M. tuberculosis (607):

Broth:

AOAC broth plus 5 per cent glycerin
pH 7.2

Agar: Dubos—modified

Sheffield Hydrolyzed Casein (N-Z-Case)	2	grams
Dibasic sodium phosphate	6.3	grams
Monobasic potassium phosphate	1.0	grams
Sodium citrate	1.5	grams
Difco Yeast extract	2.0	grams
Agar	15.0	grams
per liter		
pH 7.0 to 7.2—no adjustment necessary		

Autoclave 20 min. at 15 pounds. Before pouring plates add 10 per cent sterile oleic acid albumin complex with 5 per cent glucose (from Microbiological Associates, Inc., Coral Gables, Fla.).

In the case of *Streptococcus hemolyticus* approximately 100 million streptococci are inoculated on each slide as determined by colony count. About 90 per cent of these die during the 18 to 24 hour drying interval, so that 10 million are left when the disinfectants are applied.

In the case of *M. pyog. aureus* there were approximately 24 million organisms on each slide before drying, and approximately 5 million after drying, denoting a reduction by 80 per cent.

In the case of *M. tuberculosis* approximately one and one-half million organisms are inoculated on each slide, as determined by colony count. About 333,000 remain after drying, a loss of 78 per cent.

Results

Tables I to VI show the results of all the individual tests. As is often the case, tests with some disinfectants yield rather regular results while with others it is more difficult to ascertain their minimum germicidal concentrations.

Table VII is a summary presenting the minimum germicidal concentration of each disinfectant tested. (The germicidal dilution was considered the greatest dilution which permitted no growth in a majority of tests at that dilution.) In addition, this table shows the use-dilutions calculated from the respective declared phenol coefficients; incidentally, this "use-dilution" is presumed to involve the "safety-margin" dealt with before.

A review of the results obtained reveals a number of significant facts. In the case of phenol (carbolic acid), and of the "soluble" cresylic disinfectants Liquor Cresolis Sap. and the Cresylic Disinfectant (p. c. 5), the use dilutions are sufficiently strong to sterilize the cultures of streptococci, staphylococci and tubercle bacilli in the presence of saliva, as well as in that of saliva plus dust. By contrast, the use dilutions of the two "emulsifiable" coal-tar disinfectants do not show sufficient antibacterial power, its lack being evident particularly in all those cases in which dust is present. Nor is the recommended use dilution of the synthetic phenolic disinfectant studied sufficient to effect sterilization under these conditions, although double this concentration should be effective.

TABLE I
Strep. hemolyticus with Saliva
 Number of Colonies per Slide

Disinfectant	Dilutions	Test 1	Test 2	Test 3	Test 4
Phenol	1:60	0	0	0	0
	1:80	0	160	0	160
	1:100	6000	130,000	47,000	47,000
	1:120	200,000	650,000	400,000	
	1:160	TMTC*	TMTC		TMTC
Liquor Cresolis Saponatus	1:80	0	0	0	0
	1:100	0	80	0	0
	1:125	80	720	240	160
	1:150	560	2800		2320
	1:175		20,160		
	1:400		504,000	TMTC	TMTC
Cresylic Disinf. Fortified (p. c. 5)	1:150	0	0	0	0
	1:175	0	0	0	0
	1:200	80	20,160	18,000	300
	1:400	85,000	24,000	84,000	62,000
	1:600	TMTC	TMTC	TMTC	TMTC
Synthetic Phenolic Disinf. (p. c. 5)	1:100	0		0	0
	1:125	0	0	0	0
	1:150	0	4,000	900	240
	1:175	0	0	900	0
	1:200	80	30,000	3,000	240
	1:600	TMTC	TMTC	TMTC	
Coal Tar Disinf. Emulsif. (p. c. 7.5)	1:125	0	0	0	0
	1:150	0	0	0	0
	1:175	4,000	0	2,000	500
	1:200	6,000	0	0	5,000
	1:400	5,000	17,000	400	85,000
	1:1000	TMTC	TMTC		
Coal Tar Disinf. Emulsif. (p. c. 10)	1:200	0	0	0	0
	1:300	0	0	2,000	2,880
	1:400	0	40,000	4,000	2,000
	1:600	3,000	20,000	35,000	
	1:1000	TMTC	TMTC		
Hypochlorite Disinf. (5.2% av. Cl.)	1:60	0	0	0	0
	1:80	0	0	0	0
	1:100	3,000	0	600	1,000
	1:125	7,000	30,000	4,000	
	1:400	TMTC	TMTC		
Benzalkonium Chloride (Anhyd.)	1:1000	0	0		
	1:2000	0	0	0	0
	1:3000	0	0	0	0
	1:4000	1,400	400	400	400
	1:5000	3,000	500	1,000	320
	1:50000	TMTC		TMTC	
Benzethonium Chloride (Anhyd.)	1:2000	0	0	0	0
	1:3000	500	0	0	300
	1:4000	0	240	2,500	480
	1:6000	15,000	2,000	1,400	240
	1:8000	6,000	12,000	600	2,000
	1:50000	TMTC	TMTC		

* TMTC = Too many to count

TABLE II
Strep. hemolyticus with Saliva and Dust
 Number of Colonies per Slide

Disinfectant	Dilutions	Test 1	Test 2	Test 3	Test 4
Phenol	1:60	0	0	0	0
	1:80	160	0	900	600
	1:100	400	4000	2000	27000
	1:120		90000		100800
	1:160	TMTC	TMTC		
Liquor	1:80	0	0		0
Cresolis	1:100	0	0	0	160
Saponatus	1:125	7000	3000	1600	0
	1:150	52000		30000	240
	1:300	504000			120000
	1:400	TMTC		TMTC	
Cresylic	1:100	0	0	0	0
Disinf.	1:125	0	0	0	0
Fortified	1:150	0	0	0	0
(p. c. 5)	1:200	2640	1638	160	0
	1:400	70000	11000	116000	
	1:600		TMTC		
Synthetic	1:40	0	0	0	
Phenolic	1:60	0	800	0	0
Disinf.	1:80	0	0	0	700
(p. c. 5)	1:100	17000	6000	11000	2000
	1:400	TMTC	952000	TMTC	
Coal Tar	1:60	0	0	0	0
Disinf.	1:80	160	0	900	600
Emulsif. (p. c. 7.5)	1:100	400	4000	2000	27000
	1:200	190000	151000	85000	
	1:800	TMTC	TMTC		
Coal Tar	1:100	0	0	0	0
Disinf.	1:125	0	80	0	0
Emulsif. (p. c. 10)	1:150	3000	240	700	4800
	1:200	8000	15000	7000	1800
	1:400	176000	136000		
	1:800	TMTC	TMTC		
Hypochlorite	1:40	0	0	0	
Disinf.	1:60	0	0	0	240
(5.2% av. Cl.)	1:80	11000	160	400	7000
	1:100	48000	3500	20000	7000
	1:200	TMTC	TMTC		
Benzalkonium	1:1000	0	0	0	0
Chloride	1:2000	2600	1100	8000	2000
(Anhyd.)	1:4000	42000	28000	43000	3000
	1:10000	TMTC	TMTC		
Benzethonium	1:200	0	0		
Chloride	1:400	240	0	0	300
(Anhyd.)	1:600	1600	900	240	80
	1:800	4000	600	160	
	1:1000	9000	1000	1000	
	1:20000	TMTC	TMTC		

TABLE III
M. aureus with *Saliva*
 Number of Colonies per Slide

Disinfectant	Dilutions	Test 1	Test 2	Test 3	Test 4
Phenol	1:60	0	0	0	
	1:70	0	0	0	0
	1:80	2,500	4,100	2,000	0
	1:90	4,000		240	160
	1:175	76,000	TMTC		
Liquor Cresolis Saponatus	1:80	0	0	0	
	1:100	0	0	0	0
	1:125	5,000	240	0	160
	1:150	11,000	6,000	2,400	2,200
	1:400	800,000	TMTC		
Cresylic Disinf. Fortified (p. c. 5)	1:175	0	0	0	0
	1:200	0	0	0	0
	1:250	3,900	240	3,520	
	1:600	161,000			880,000
	1:800	TMTC			
Synthetic Phenolic Disinf. (p. c. 5)	1:80	0	0	0	0
	1:100	0	0	0	0
	1:125	2,000	16,000	1,700	0
	1:600	76,000	TMTC		
Coal Tar Disinf. Emulsif. (p. c. 7.5)	1:100	0	0	0	0
	1:125	0	0	0	
	1:150	0	0	720	0
	1:200	80	1,440	13,000	160
	1:800	177,000	105,800		
Coal Tar Disinf. Emulsif. (p. c. 10)	1:150	0	0	0	0
	1:200	1,700	160	240	240
	1:400	6,800	320	15,120	6,700
	1:1000	770,000	756,000	TMTC	TMTC
Hypochlorite Disinf. (5.2% av. Cl.)	1:40	0	0	0	0
	1:60	160	0	0	0
	1:80	3,000	1,800	80	2,400
	1:100	2,900	35,000	3,000	11,000
	1:200	TMTC	453,000	TMTC	
Benzalkonium Chloride (anhyd.)	1:2000	0	0	0	0
	1:4000	0	0	0	0
	1:6000	80	900	53,000	80
	1:40000	90,000	248,000	680,000	201,000
	1:60000	TMTC			
Benzethonium Chloride (anhyd.)	1:1000	80	0	0	0
	1:2000	0	160	0	0
	1:4000	0	1,800	560	700
	1:40000	383,000	196,000	151,200	105,800
	1:60000	TMTC			

TABLE IV
M. aureus with Saliva and Dust
 Number of Colonies per Slide

Disinfectant	Dilution	Test 1	Test 2	Test 3	Test 4
Phenol	1:70	0	0	0	0
	1:80	880	160	0	0
	1:100	400	80	1,440	
	1:175	352,000			TMTC
Liquor	1:80	0	0	0	0
Cresolis	1:100	0	0	0	0
Saponatus	1:125	720	160	0	1,100
	1:600	181,000	160,000	TMTC	
Cresylic	1:175	0	0	0	0
Disinf.	1:200	2,000	80	2,000	320
Fortified (p. c. 5)	1:600	234,000	1,040,000		
	1:800	TMTC	TMTC		
Synthetic	1:80	0	0	0	0
Phenolic	1:100	0	0	0	0
Disinf. (p. c. 5)	1:125	2,000	1,200	12,000	
	1:200	1,900	55,000		960
	1:400	648,000	TMTC	252,000	141,000
Coal Tar	1:80	0	0	0	0
Disinf.	1:100	0	80	0	240
Emulsif. (p. c. 7.5)	1:600	442,000	240,000	17,000	
	1:800	2,000,000	287,000	35,200	105,000
Coal Tar	1:150	0	0	0	0
Disinf.	1:200	320	160	2,000	6,000
Emulsif. (p. c. 10)	1:600	25,000	1,600,000	20,000	3,600
	1:800	493,000		1,200,000	
Hypochlorite	1:40	0	0	0	0
Disinf. (5.2% av. Cl.)	1:60	1,600	2,500	480	2,000
	1:80	13,000	6,700	9,600	2,200
	1:100	221,000	3,200	307,400	
	1:400	166,000	1,200,000	760,000	TMTC
Benzalkonium	1:600	0	0	0	0
Chloride	1:800	0	400	80	2,000
(anhyd.)	1:1000	880	960	640	2,200
	1:2000	48,000	3,200	23,000	
	1:20000	TMTC	448,000	378,000	
Benzethonium	1:600	0	0	0	0
Chloride	1:800	4,700	320	240	240
(anhyd.)	1:1000	2,600	2,200	1,100	320
	1:2000	14,000	7,000		
	1:20000	60,000	100,000	201,600	
	1:40000	227,000	468,000	TMTC	504,000

TABLE V

M. tuberculosis with Saliva
Number of Colonies per Slide

Disinfectant	Dilution	Test 1	Test 2	Test 3	Test 4
Phenol	1:60	0	0	0	0
	1:80	3,200	0	1,200	80
	1:100	24,000	5,000	4,000	2,800
	1:120	TMTC	11,000		156,000
Liquor Cresolis Saponatus	1:100	0	0	0	
	1:125	0	0	0	80
	1:150	480	0	560	160
	1:200	6,000	80	7,000	3,000
	1:600		18,000	TMTC	
	1:800	TMTC			
Cresylic Disinf. Fortified (p. c. 5)	1:175	0	0	0	0
	1:200	80	0	0	0
	1:300	3,500	2,000	240	2,000
	1:400	6,800	6,000		
	1:1000	121,000	222,000	121,000	
Synthetic Phenolic Disinf. (p. c. 5)	1:100	0	0	0	0
	1:125	640	0	0	400
	1:150	12,000	0	80	8,000
	1:200	35,000	6,000	1,300	
	1:400	18,000	244,000	84,000	
Coal Tar Disinf. Emulsif. (p. c. 7.5)	1:100	0	0	0	0
	1:125	0	0	0	240
	1:150	160	2,800	80	80
	1:200	480	2,900	560	
	1:600	178,000	23,800	40,000	
Coal Tar Disinf. Emulsif. (p. c. 10)	1:175	0	0	0	0
	1:200	0	2,000	0	4,000
	1:300	640	44,000	640	1,800
	1:400	15,000		7,000	46,000
	1:800	TMTC		72,000	
Hypochlorite Disinf., (5.2% av. Cl.)	1:20	0	0	0	
	1:40	320	80	0	0
	1:60	800	1,600	400	480
	1:100	2,000	110,000	4,000	
Benzalkonium Chloride (anhyd.)	1:80	0	0	0	160
	1:100	0	0	160	0
	1:200	900	8,000	10,000	160
	1:400	18,000	44,000	24,000	160
	1:2000	47,000			
Benzethonium Chloride (anhyd.)	1:10	0	0	160	0
	1:20	800	0	4,000	160
	1:40	2,000	1,200	3,000	1,400
	1:600	80,100	34,000		

TABLE VI
M. tuberculosis with Saliva and Dust
 Number of Colonies per Slide

Disinfectant	Dilution	Test 1	Test 2	Test 3	Test 4
Phenol	1:60	0	0	0	
	1:80	0	80	1,100	80
	1:100	1,000	1,600	54,000	30,000
	1:120	3,600			167,000
	1:200	206,000			
Liquor Cresolis Saponatus	1:100	0	0	0	
	1:125	0	0	880	0
	1:150	2,000	0	3,500	80
	1:200	3,000	240	36,000	1,400
	1:600	16,100	20,600		
	1:800	TMTC			
Cresylic Disinf. Fortified (p. c. 5)	1:175	0	0	0	
	1:200	0	0	80	80
	1:300	4,000	2,000	80	19,000
	1:600	48,000	32,000	64,000	
	1:800	51,000	10,000	207,000	
Synthetic Phenolic Disinf. (p. c. 5)	1:60	0	0	0	0
	1:80	160	0	320	0
	1:100	300	80	400	300
	1:200	20,000	20,000	105,000	1,600
	1:400	54,000	206,000		11,000
Coal Tar Disinf. Emulsif. (p. c. 7.5)	1:80	0	0	0	
	1:100	0	0	240	0
	1:150	80	320	800	31,000
	1:400	1,400	2,000	39,000	
	1:600	TMTC		182,000	
Coal Tar Disinf. Emulsif. (p. c. 10)	1:125	0	0	0	0
	1:150	600	1,200	0	0
	1:200	1,000	23,000	160	400
	1:400	37,000			14,000
	1:600	55,000		80,000	
Hypochlorite Disinf. (5.2% av. Cl.)	1:20	0	0	0	0
	1:40	160	80	400	16,000
	1:60	800	1,200	1,700	140,000
	1:100	7,000			176,000
	1:200	302,000	24,000		
Benzalkonium Chloride (anhyd.)	1:60	0	0	0	160
	1:80	0	320	0	0
	1:100	0	900	320	480
	1:200	160	3,000	0	6,000
	1:1000	77,000	36,000		
Benzethonium Chloride (anhyd.)	1:10	0	160	0	0
	1:20	0	960	800	160
	1:40	2,000	3,000	4,000	1,700
	1:100	3,000	25,000	44,000	27,000
	1:400	54,000	222,000		

TABLE VII
SUMMARY OF DILUTIONS GERMICIDAL IN 10 MINUTES

	<i>Strep. hemolyticus</i>		<i>M. aureus</i>		<i>M. tuberculosis</i>		Use Dilution (20 x <i>S. typhosa</i> p. c.)
	With Saliva	With Saliva & Dust	With Saliva	With Saliva & Dust	With Saliva	With Saliva & Dust	
Disinfectant							
Phenol	1:60	1:60	1:70	1:70	1:60	1:60	1:20
Liquor Cresolis	1:100	1:100	1:100	1:100	1:125	1:125	1:40
Saponatus							
Cresylic Disinf., fortified (p. c. 5)	1:175	1:150	1:200	1:175	1:200	1:175	1:100
Synthetic Phenolic Disinf. (p. c. 5)	1:125	1:80	1:100	1:100	1:100	1:60	1:100
Coal Tar Disinf., Emulsif. (p. c. 7.5)	1:150	1:60	1:150	1:100	1:125	1:100	1:150
Coal Tar Disinf. Emulsif. (p. c. 10)	1:200	1:125	1:150	1:150	1:175	1:125	1:200
Hypochlorite Disinf. (5.2% av. Cl.)	1:80	1:60	1:60	1:40	1:120	1:20	1:166*
Benzalkonium Chloride (Anhyd.)	1:3000	1:1000	1:4000	1:600	1:100	1:80	1:5000
Benzethonium Chloride (Anhyd.)	1:2000	1:200	1:2000	1:600	1:10	1:10	1:4000

* No. p. c. quoted on label, but this dilution is recommended for cleaning floors.

The greatest extent of impairment of antibacterial action by saliva and dust is encountered in the case of the hypochlorite disinfectant and in that of the quaternary ammonium compounds. This is due probably to two different causes. In the former case, the oxidative reactivity of the hypochlorite with the organic matter present in dust and saliva deflects a substantial portion of the antibacterial potential from its proper function. In the latter case, the characteristic and pronounced surface action of the quaternary ammonium compounds is responsible for their strong adsorption upon the dust and saliva particles, thus reducing their availability for action upon the microorganisms present.

Supplementary Tests

In view of the weak performance of the two quaternary ammonium compounds, particularly with respect to *M. tuberculosis*, we decided to carry out a supplementary test using the AOAC technic except for the following modifications necessitated by the use of this test organism. The test culture of *M. tuberculosis* (607) was grown in AOAC broth plus 5 percent of glycerine (pH 7.0 to 7.2) for one week at 37° C. Clumps were broken up by rapid pipetting, and the culture was filtered through a 200 mesh sieve. Tests were made at 20° C., and at the 10 minute interval only. The subculture medium consisted of the above broth plus 0.05 percent of Tween 80. "Shippen subtransfers" were made into the same broth.

The phenol resistance of the culture used is shown below (10 minutes, 20° C.):

1:60 —

1:70 +

The results of the tests with the quaternary ammonium compounds are given in the following table:

TABLE VIII
Germicidal Tests—*M. tuberculosis*
20° C.—10 minute Medication Interval

Dilutions	Benzalkonium Chloride		Benzethonium Chloride	
	Subtransfer		Subtransfer	
	10 min.	from 10 min.	10 min.	from 10 min.
1:10	—	—	—	+
1:100	—	+	—	+
1:200	—	+	+	+
1:400	—	+	+	+
1:600	—	+	+	+

The Shippen subtransfer (of 4 loopfuls from the subculture tube into a fresh tube of medium) serves the purpose of reducing or eliminating bacteriostasis by further diluting the disinfectant transferred with the subculture inoculum.

The above findings show that the first subtransfer does not dilute the disinfectants to a point below their bacteriostatic range. By reducing or eliminating bacteriostasis, concentrations as high as 10% of benzethonium chloride are found to be incapable of sterilizing the culture of *M. tuberculosis*, while in the case of benzalkonium chloride there appears to exist a considerable latitude between the bacteriostatic and bactericidal ranges.

Summary

A review of recent literature tends to emphasize the position which the "secondary reservoirs" hold in the spread of respiratory infections. Sedimented pathogenic organisms which have been expelled originally by some mode of forced respiratory action are stirred up from these reservoirs by air currents and contaminate the air of enclosed spaces; in turn this leads to infections through the nasopharyngeal portal of entry.

Since the pathogens of the secondary reservoirs may be presumed to be protected by dried salivary mucus and by ordinary dust, an attempt was made to study the antibacterial performance of several disinfectants in the presence of these factors. *Strep. hemolyticus*, *Staph. pyog. aureus* and *M. tuberculosis* were used as test organisms because of their preëminence in the secondary reservoirs of respiratory pathogens.

With the aid of special methods intended to approximate practical use conditions, it was found that salivary mucus and ordinary dust affect the performance of different disinfectants in varying degrees. Specifically, the recommended dilutions for use, as derived from the respective AOAC phenol coefficients, were found to be sufficiently strong to kill the streptococci, staphylococci and tubercle bacilli, in the case of phenol (carbolic acid). Liquor Cresolis Saponatus and Cresylic Disinfectant (p. c. 5). The use dilutions of two emulsifiable coal tar disinfectants did not show sufficient antibacterial power, its lack being evident particularly in those cases in which dust was present.

The greatest extent of impairment of antibacterial action by saliva and dust was encountered in the case of the hypochlorite disinfectant, and in that of the quaternary ammonium compounds.

The latter were retested in the absence of any interfering factors, with *M. tuberculosis* as test organism. Reduction of bacteriostasis by means of subtransfers showed these compounds to be possessed of a rather weak tuberculocidal power.

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EFFECT OF ANTIHISTAMINES ON VIRUSES OF THE INFLUENZA GROUP *

By Julian L. Ambrus, Clara M. Ambrus and
Joseph W. E. Harrison
(with the assistance of Howard
Cravetz and Arthur E. Greene)

SINCE the first reports of Brewster (1) on the beneficial results of antihistamines in common cold, his results have been confirmed by several authors (2, 3, 4, 5), criticized by others (6), and presumably disproved by still others (7, 8, 9). The contradiction of these findings may lie partly in the difficulty of the clinical diagnosis of the common cold, which may be easily mistaken for various nasal allergies, infections of the respiratory tract, local irritations, influenza, abortive measles, etc. The possible virus character of the causative agent of the common cold has been demonstrated by Dochez *et al.* (10), Topping and Atlas (11) and others. The latter authors demonstrated that this virus may not be identical with influenza virus. There is only one investigation employing antihistamines (8) in which cases of "spontaneous" colds have been used along with colds experimentally produced by intranasal inoculation of the cold virus into human volunteers.

The aim of the present investigation was to study the effect of antihistamines on influenza and New Castle-disease virus.

Methods

The PR8 influenza A, the Lee strain of influenza B and the California No. 11914 strain of New Castle disease virus were used. The influenza viruses were inoculated into 10 day old and the New Castle disease virus into 12 day old embryonated leghorn eggs by injection into the allantoic cavity in 0.1 ml. of normal saline. The drugs when administered were also injected into the allantoic cavity in 0.2 ml. of physiological saline.

Control embryos received different multiples of I. D.₅₀ doses of virus and test embryos the same doses following the previous ad-

* From the LaWall Memorial Laboratory of Pharmacology and Biochemistry, Philadelphia College of Pharmacy and Science.

ministration of 1 or 2 mg. of the antihistamine. The viruses employed were previously evaluated in the following manner: Titrated for hemagglutinins and for I. D.₅₀, then immediately lyophilized. When the I. D.₅₀ test was read either 24 or 48 hours later, the lyophilized virus was thawed and again titrated for hemagglutinins. Doses to be administered were calculated on the basis of the found I. D.₅₀ corrected for any change in hemagglutinin titer as shown by the first and second titers.

We considered this a more dependable method of assuring a constant value for the infecting virus than most commonly used simpler procedures.

The study embryos were incubated at 37° C. in the instance of influenza inoculation for 48 hours, and for 24 hours in New Castle diseases. After this period the eggs were candled and survivals or death recorded. Subsequently, they were chilled at +4° C. for three hours, the allantoic fluid harvested and titrated for hemagglutinins. Hemagglutination tests were performed according to the modifications of Salk (12) and Lepine (13) of Hirst's method (14). 1 ml. of 0.5% suspension of washed chick red blood cells was added to 1 ml. of allantoic fluid. If hemagglutination did not occur within one and a half hours, the virus was regarded as absent. If hemagglutination occurred the same procedure was repeated using a dilution series of the allantoic fluid ranging from 1:5 to 1:10290. Hemagglutination was read by the pattern method of Salk (12). The end point was considered to be the highest dilution showing complete agglutination.

Viability of the viruses present was determined in the following manner; Allantoic fluids of each group, showing hemagglutinins, were pooled and titrated for infectivity using 5 embryos per dilution. Allantoic fluids showing no hemagglutinins were injected in a similar manner, undiluted into each of 5 embryos.

The following antihistamines were tested: *

Neoantergan	(Rhône Poulenc)
3277RP	(Rhône Poulenc)
3015RP	(Rhône Poulenc)
Benadryl	(Parke, Davis Co.)
Thephorin	(Hoffmann-LaRoche)
Antistine	(Ciba)

* We are greatly indebted to the manufacturers for supplying us with these drugs.

Results

"In Vivo" Effects:

Neither 1 nor 2 mg. of the antihistamines significantly affected either influenza or New Castle disease virus when these viruses were administered in doses of 2, 10 or 100 I. D.₅₀. Viability tests demonstrated that when the agglutination was positive the infection was transferable to other embryos, thus a decrease in the infectivity value was not evident.

"In Vitro" Effects:

1 mg. of the antihistamines in 0.05 ml. of physiological saline, admixed with 0.05 ml. of saline containing 10 I.D.₅₀ of the respective viruses, incubated for 2 hours at 37° C., then injected into the allantoic cavity did not result in any demonstrable decrease of infectivity.

Summary

The antihistamines employed apparently have no effect on the multiplication and infectivity of influenza A or B, or of New Castle-disease viruses in the chick embryo. Nor was any effect observed on these viruses by *in vitro* incubation tests. The results in themselves do not necessarily mean uselessness of antihistamines in influenza as they may act, e. g., on concomitant allergic phenomena, on capillary permeability and other factors that may be involved.

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THE HISTORY OF RETAIL PHARMACY IN THE CITY OF BROOKLYN TO 1830.

By Herbert C. Raubenheimer*

IN the various books on the History of Pharmacy there is no mention of the beginnings of this profession in the City of Brooklyn. We have a record of the early pharmacies of the English colonies, of the City of Philadelphia, and of New York City, but none of "The City of Churches." I have devoted considerable time to collecting a record of the early practice of retail pharmacy in Brooklyn and the results of my findings are herewith presented.

The first apothecary shops in America were dispensaries of medical practitioners, who had their offices behind the shops which were attended by an apprentice physician, called "apothecary," who in time might qualify himself to engage in the unregulated and unlicensed business of medicating the community on his own account (1). This same situation occurred in the early history of pharmacy in the City of Brooklyn.

Until the close of the Indian War of 1643, the colonists on Long Island were dependent for medical treatment on the surgeons that accompanied the ships of the Dutch West Indies Company. A company of soldiers from Curacao brought with them Paulus Van der Beeck who was destined to become the first practitioner in Kings County (2). From this start other physicians came to Brooklyn and practiced medicine and pharmacy. In this paper I am not concerned with tracing medical history and have devoted myself to the early history of retail pharmacy.

The first record of a retail pharmacy, that I could find, in Brooklyn was Kaempf's German Pharmacy in 1799. It was conducted by Charles Kaempf at 149 Atlantic Avenue between Henry and Clinton Streets. He was succeeded by his son, Charles L. Kaempf and he by his nephew, Lewis Lehn. "Uncle Kaempf's Corn Salve," a popular remedy of the day, was manufactured there. In 1874, Louis Lehn helped to found the wholesale firm of Lehn and Fink and he sold the Brooklyn store to Schleussner and Syvarth (3).

* Professor of Pharmacy, St. John's University, College of Pharmacy, Brooklyn, N. Y.

We come to the turn of the century for the next recording of a retail pharmacy in Brooklyn. It is of interest to note that the town of Brooklyn had a population of 3,298 in 1800; 4,402 in 1810 and 7,175 in 1820 (4). Among the first of the druggists in Brooklyn in the early part of the nineteenth century was Dr. Osborn, whose "apothecary shop" was bought in 1811 by Ithiel Smead and continued for a number of years (5). In 1818, E. Hall opened a drug store at 119 Atlantic Avenue, on the northwest corner of Henry Street. He conducted this establishment until 1836 and then it was owned by W. Ayers until 1848 (6).

Dr. Charles Ball and Dr. Matthew Wendell were partners who began their Brooklyn practice early in the nineteenth century, and maintained an office for the dispensing of drugs at the corner of Fulton and Sands Streets (7). This was in 1816 and both, in 1822, were founders of the Kings County Medical Society (8). Also in 1816, John Valentine Swertcope, a Hessian soldier who served with the British Army in the Revolution, did a considerable business in the distilling of Rose Water. Roses, at that time, were raised in great abundance in the gardens of Brooklyn, and many persons were accustomed to send their annual crop of rose leaves to Swertcope who returned to each customer one-half of the yield in Rose Water (9).

In 1820, Dr. Joseph Gedney Tralton Hunt had an office and a drug shop at Concord and Fulton Streets (10). About this time a Dr. Henderson "lately from Edinburgh" opened a medical store on Fulton Street and offered his services (7). He also had an advertisement in the October 11, 1821 issue of "The Star", a weekly paper of that time, wherein he "begs leave to inform the inhabitants and vicinity of Brooklyn, that he has opened a medical store corner Main and Fulton Streets, where all kinds of medicine may be had at primitive purity, at New York prices" (11). It seems that purity and price were a factor at that early date.

The next record of a retail pharmacy that I could find was the pharmacy of John J. Cole, Jr.; located at 94 Fulton Street, in 1822 (12). For a personal reason, I was interested in finding more information regarding this store but after considerable research I could not obtain any additional data on this establishment. I might mention here, that in 1822 Brooklyn also had a drug and dye manufactory (13).

In 1825 we find the first of our "modern" pharmacies. It was operated by J. V. E. Vanderhoef and was located at 108 Fulton Street (14). Vanderhoef was listed in the *Brooklyn Directory* each year until 1838. He advertised extensively in the *Brooklyn Directory* and in *The Star*. It might be of interest to quote one of his advertisements in *The Star*. In the April 7, 1825 issue of that paper he advertised as follows:

Drugs, Medicine and Perfumery—J. V. E. Vanderhoef—
95 Fulton Street—Brooklyn. Assortment of Drugs, Medicines
and Perfumes—sell as low as can be purchased in New York.
Families may rely on procuring genuine articles at above place.
Patent Medicines—Steers Chemical Opodeldoc—Whitwell's
Chemical Embrocation—Whitwell's Aromatic Snuff—Cephalic
Snuff—Soda Powders—British Oil—Harlem Oil—Bateman's
Drops—Godfrey's Cordial—Seidlitz Powders.

Double Distilled Rose Water—wholesale and retail.

Wanted: a smart active boy, 14 or 15 years of age, of respectable connections, to attend drug store.

This advertisement appeared weekly in *The Star* and the ad for the "smart boy" appeared from the April 7, 1825 issue through April 28, 1825 (15). Perhaps help was scarce at that time. These advertisements of Vanderhoef's also indicated that price was a factor, as it is today, and it also emphasized the "procuring of the genuine article". This store was the "most frequented" drug store of that time (16).

Vanderhoef soon expanded and opened another store. In the December 29, 1825 issue of *The Star*, in addition to his regular advertisement, he had a notice that "he has opened and established a store for the sale of Drugs, Medicines and Perfumery at 107 Sands Street, near Bridge" (17). In the 1826 and 1829 issues of the *Brooklyn Directory* both the Fulton Street and Sands Street locations were listed (18).

In 1828 Brooklyn had a dentist who kept a drug store at 2 Sands Street. An advertisement of his reads in part, "he would recommend Persian Dentrifrice, kept by him, to all those who are desirous of having their gums healthy and teeth white and clear from Tartar without any injury to either. Also a general assortment of Drugs, Medicines and Perfumery for sale" (19). It seems that perfumery was an important part of the stock of the druggist of that time.

I might also add that Alden Spooner, publisher of *The Star*, also dealt in drugs and other merchandise besides publishing his newspaper. He sold these items at his office at 50 Fulton Street. In one of his numerous advertisements of his retail stock, Spooner announced that a "fresh supply of Hair Restorative and Preservative Vegetable Cerate was on hand" (20). In looking through the various issues of *The Star* I noted the following drug items that he advertised and sold at his office: Marshall's Infallible Remedy for Piles, Podadelphis, The India Extract for Rheumatism, etc.; Dr. Cowell's Odontalgia and Dr. Angelis Pills.

Among other persons who had drug stores in Brooklyn at that time, though no further information concerning them could be found were: G. Skenst, at Johnson Street and George F. Mountain at Adams Street (21).

This concludes the listing of pharmacists who operated a retail pharmacy in Brooklyn, as far as my research could trace, until 1830. If anyone has any information on any other drug stores operating in Brooklyn prior to 1830 the writer would be most pleased to hear about them. [My next paper will deal with the retail pharmacies in Brooklyn from 1830 to 1840.]

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SELECTED ABSTRACTS

Sulfonamide Mixture Therapy. Lehr, D. *Brit. Med. J. No.* 4679:601 (1950). The toxicity of most of the soluble sulfonamides lies in the supersaturation of the sparingly soluble sulfonamide or its metabolic product in the urine with the resulting deposition of crystals in the renal pathways, known as crystalluria. The use of mixtures reduces the danger of crystalluria because each sulfonamide is soluble at the same time to the full extent of its individual solubility. Since the therapeutic effectiveness of the components of the mixture is additive each need be present as only a fraction of its individual dose and therefore the urinary level of the individual sulfonamide need not exceed its solubility.

Some have thought that the use of mixtures will increase the development of sensitization with sensitivity simultaneously developing against more than one member of the mixture. Such an effect would reduce the possibility of switching a sensitized patient to another sulfonamide. This concept was based upon the expectation that the incidence of sensitization was largely independent of dose. However, recent studies have shown that the production of sensitization is dependent upon the repeated presence of certain minimal tissue concentrations of the sulfonamide for a minimum period of several days.

Sulfadiazine was shown to be the least plasma-bound, best diffusing, and least acetylated of the group including sulfamerazine, sulfamethazine, and sulfapyrazine. Sulfathiazole showed lower blood levels and poor diffusion into the cerebral spinal fluid. Sulfacetamide, although having low blood levels due to rapid excretion, exceeded the advantages of sulfadiazine in regard to diffusion into the cerebro-spinal fluid and plasma binding. No substantial differences seem to exist among the soluble sulfonamides as to their bacterial spectrum. Molecular changes at the N₁ position seem only to cause a quantitative difference in antibacterial properties. Animal toxicity test showed sulfathiazole to be most toxic followed by sulfapyrazine, sulfadiazine, sulfamerazine, sulfamethazine and sulfacetamide. The latter was only one fifth as toxic as sulfadiazine.

The author concluded that sulfadiazine and sulfamerazine qualified for first and second place in sulfonamide mixtures with sulfa-

thiazole, sulfapyrazine, sulfamethazine, and sulfacetamide deserving attention as possible additional members of mixtures. Sulfacetamide as the third member of a mixture tends to raise the blood levels slightly within the first four hours and to lower them thereafter while sulfamethazine in the same position assists in the prolongation of high levels with a retardation of urinary excretion. Clinical trials in 170 patients with various acute systemic infections using a mixture of equal parts of sulfadiazine, sulfamerazine and sulfacetamide showed a high curative value and low toxicity.

Scarlet Fever Therapy. Weinstein, L. and Potsubay, S. F. *J. Pediat.* 37:291 (1950). A comparison of treatment in 255 patients with scarlet fever ranging in age from 1 to 57 years was made by the authors. The patients were divided into three groups according to the treatment given. Group I received symptomatic treatment consisting of such measures as bed rest and throat irrigations. The patients in group II received 1 intramuscular injection of 20 to 60 cc. of a γ -globulin solution having a potency of 30 to 80 anti-erythrocytic units per cc. Group III patients received 15,000 units of penicillin intramuscularly every 3 hours for 10 days. There were 102 patients in group I, 103 in group II and 50 in group III.

The result of treatment was reported in the following manner. The temperature returned to normal within 24 hours in 24.5 per cent of the patients in group I, in 11.65 per cent of group II, and in 48 per cent of group III. Within a period of 4 days 94 per cent of group III had a normal temperature, 70.5 per cent of group I and 67.9 per cent of group II. Pain in the pharynx was completely relieved within 1 to 3 days in the patients in group III but lasted an average of 6 days in the patients in the other two groups. The rash disappeared within 24 to 36 hours in the patients in group II but lasted for $4\frac{1}{2}$ days in the patients in groups I and III. The white blood cell count had returned to normal and *Streptococcus pyogenes* had disappeared from the pharynx in 96 per cent of the patients in group III within 1 week but the patients in the other two groups lagged considerably behind. Subsequent results of the disease were much less significant in group III. There was no evidence of suppurative sequelae in this group but the treatment given to the patients in group II seemed to have no effect on the incidence of suppurative sequelae nor on such other sequelae as rheumatic fever.

Treatment of Neurosyphilis. Johnwick, E. B. *J. Ven. Dis. Inform.* 31:303 (1950). An evaluation of the effect of adding arsenicals and bismuth to a schedule of penicillin for the treatment of neurosyphilis was presented by the author. The first treatment schedule (0-60-0) consisted of 400,000 units of penicillin administered intramuscularly in peanut oil and beeswax each day for 15 consecutive days. The second schedule (8-60-5) consisted of the penicillin plus 0.06 Gm. of Mapharsen on the odd days of treatment and $1\frac{1}{2}$ cc. of bismuth subsalicylate in oil on the first, third, fifth, tenth, and fifteenth days. A total of 619 patients were treated on the 0-60-0 schedule and 260 patients on the 8-60-5 schedule.

The initial cerebrospinal fluid cell count averaged 38.3 for the 0-60-0 group and 50.3 for the 8-60-5 group, among those patients who did not require re-treatment. The average initial count among the 16 requiring re-treatment in the 0-60-0 group was 42 with 6 having counts of over 50. The average initial count among the 21 requiring re-treatment in the 8-60-5 group was 88.1 with 15 having counts over 50. In view of these findings and of the fact that approximately the same percentage in each schedule group had a duration of the disease of over 4 years, the author suggested that the cell count provided a better prognostic sign than did the age of the infection.

Following treatment among the patients not requiring re-treatment in both schedule groups the cell count dropped to normal and remained there for 18 months. During the same 18 month period the quantitative Kahn serological tests among the same patients were practically the identical for both schedule groups, having dropped from an over-all average of 114.6 Kahn titer units to 12.4 titer units. Therefore, the author concluded that nothing was gained by the addition of the Mapharsen and the bismuth to the penicillin treatment schedule.

The Bactericidal Action of Penicillin. Eagle, H., Fleischman, R., and Musselman, A. D. *Ann. Internal Med.* 33:544 (1950). *Diplococcus pneumoniae* types I and III and groups A and B of β -hemolytic streptococci responded to penicillin in *in vitro* and *in vivo* studies performed by the authors. The direct action of penicillin was studied by the determination of the survival time in inoculated

muscles of mice with organisms not previously exposed to penicillin and with organisms exposed to penicillin for 1 to 3 hours prior to inoculation. Studies were also made by the determination of the LD50 in mice for a culture before and after exposure to penicillin and after varying periods of time allowed for recovery from the exposure to penicillin. Simultaneous injections of penicillin were given to the mice when organisms were used in the inoculations which had not previously been exposed to penicillin *in vitro*. When the maximum effective levels of penicillin were employed 99.9 per cent of group A streptococci and of types I and II pneumococci were killed *in vitro* in 1½ to 3, 3 to 4, and 3 to 4 hours, respectively, and *in vivo* in 4, 5, and 3 hours, respectively. The recovery period before the surviving organisms resumed multiplication was 2 to 3 hours *in vitro* and 3 to 5 hours *in vivo*. The maximum recovery period was obtained when a concentration of 0.064 micrograms of penicillin was maintained at the intramuscular focus for a period of 1 hour. Longer exposure nor exposure to higher concentrations did not prolong the recovery period. The organisms were noted to be more susceptible to attack by the host during the recovery period before natural resistance had been regained.

The group B streptococci showed a slower zonal susceptibility to penicillin with a prolongation of the bactericidal effect long after effective antibiotic levels had disappeared. The organisms continued to die for 24 to 48 hours after exposure to a dose which provided effective penicillin levels for only about 1 hour. During the recovery period for these bacteria the LD50 value was observed to increase about 500-fold over its pretreatment value. Apparently about 99 per cent of the surviving organisms were killed by the host during the time interval before normal resistance was recovered.

Absorption of Vitamin B₁₂ in Pernicious Anemia. Ungley, C. C. *Brit. Med. J.* No. 4685:905 (1950). The author presented a series of four papers dealing with the absorption of vitamin B₁₂. By way of introduction he pointed out that vitamin B₁₂ has added further clarity to Castle's hypothesis that an intrinsic (gastric) factor and an extrinsic (food) factor interact to form the anti-pernicious-anemia factor stored in the liver. This heat stable substance fulfills the criteria of a true liver active principle in that it is effective in the

therapy of both pernicious anemia and in subacute combined degeneration of the spinal cord. On the other hand, when administered orally it behaves like the extrinsic factor in that small amounts are effective only when accompanied by a good source of intrinsic factor.

The absorption of the vitamin without an accompanying source of intrinsic factor was studied by comparing the effective oral dose with the parenteral dose that could be expected to produce a similar hemopoietic response in 15 days. This ratio was several hundred to one with ordinary doses ranging from 5 to 80 micrograms daily for as much as 24 days. However, a single dose of 3,000 micrograms in 5 patients produced a response equivalent to 80 to 160 micrograms parenterally. These surprising results would suggest that some vitamin B₁₂ can be absorbed without first combining with the intrinsic factor, if the dose is large enough. It was assumed that there was little or no intrinsic factor present because of the usual low quality and quantity of gastric secretion in patients with pernicious anemia.

When normal human gastric juice was administered along with the vitamin orally it was found that at least 500 cc. were required to produce an adequate hemopoietic response from 50 to 80 micrograms of vitamin B₁₂. However, one of the 8 patients in this series failed to respond and 2 showed an apparent absorption of only about 10 per cent of the vitamin. In view of these findings it is evident that the gastric secretion of the average pernicious anemia patient would be totally unable to provide sufficient intrinsic factor for the effective absorption of vitamin B₁₂.

Neither fresh milk nor a whey concentrate were effective substitutes for normal human gastric juice as a source of intrinsic factor.

The fourth paper presented the results of a study to determine whether or not vitamin B₁₂ without intrinsic factor would be effectively absorbed if the possibly destructive effects of intestinal contents could be avoided. The vitamin was applied to the duccal mucosa, instilled into an isolated, washed segment of intestine, and administered orally after partial sterilization of the intestine with phthalylsulfathiazole, aureomycin, and dihydrostreptomycin. All of the results were negative. In each case the subsequent administration of the vitamin with gastric juice produced a response in the patient. The author pointed out that these findings do not support but neither do they rule out the hypothesis that Castle's intrinsic factor acts by protecting vitamin B₁₂ from destruction in the gastro-intestinal tract.

BOOK REVIEWS

Botanik der Gegenwart and Vorzeit in Culturhistorischer Entwicklung. Ein Beitrag zur Geschichte der Abendländischen Völker. Von Karl F. W. Jessen (1864). 1948, Waltham, Mass., U. S. A. Republished by The Chronica Botanica Co.

Chronica Botanica has published two botanical books, or books, related to biology in the original German language. The first one has the title mentioned above, the second one has the title *Biologie der Goethe—Zeit*, edited by Adolph Meyer-Abich, Ph. D., Hamburg.

One of the greatest services of Chronica Botanica is the republishing of the book of K. F. W. Jessen in the German language, not only on account of its most interesting contents, which, although to a certain degree obsolete, are now available to modern scientists, but also for the beautiful German which German scientists, like Jessen or Oskar Peschel, Wilhelm Heydt and others used about one hundred years ago. This book is not only recommended to the botanical scholar, but also to the student of the German language.

The book is divided into twenty chapters, starting with the oldest botanical observations in Indian temples (East India), and ending with F. Darwin, a contemporary of Jessen. At the end, the book contains three tables: Table I shows the development of the plant systems, Table II has a list of the botanical literature at the time of Jessen, and Table III gives a review of the botanical journeys until 1860. It gives the names of the travelers, their native country and which parts of the world they visited.

As mentioned, the book contains a great deal of the history of civilization. Very noteworthy is what Jessen writes about the origin of the word "botany" (in German "Botanik"). It goes back to St. Basilus (315-379 A. D.). The Greek word which sounds like "votany" originally meant the low herbs of the pastures, das "kurze Weidekraut," and the original meaning of the work Botanik is in German "Kräuterkunde."

THEODOR P. HAAS

Handbook of Bacteriology, Sixth Edition. By Joseph W. Bigger. 547 pages, 1950, Baltimore. The Williams and Wilkins Company.

This volume, as were all previous editions, is intended for students and practitioners of medicine rather than for bacteriologists. The first edition appeared in 1925 and the fifth edition was published in 1939. The last decade witnessed many advances in microbiology in various fields. All chapters in the sixth edition, therefore, have received additions, deletions or alterations. Eleven have been completely rewritten and two new chapters have been added.

Though the reviewer has had other editions in his laboratory, using them as reference books, he feels that the student in the United States may obtain information needed by him from other volumes more suitable for his purpose. This comment is not made in any spirit of antagonism. However, Dr. Bigger, professor of bacteriology and preventive medicine at the University of Dublin, obviously imparts much data of greatest value to those in Great Britain, without considering the methods and procedures most commonly used in our country.

British terminology is used throughout. Culture media and methods of analyses (especially for water, milk, shellfish and disinfectants) as used in Great Britain are mentioned or detailed. The following considers a few of these. The A. P. H. A. Standard Methods for Dairy Products and for Water and Sewage and procedures for shellfish examination are accepted in this country, yet nothing is mentioned about them in this volume. The Rideal Walker test for obtaining a phenol coefficient of a disinfectant is detailed, but in our country the F. D. A. technique is used more frequently. Furthermore, a battery of many varied tests is generally used in the United States for evaluating antibacterial efficiency. In this country, the F. D. A. technique for determining the potency of penicillin and other antibiotics is followed. Certified Stains (certified by Biological Staining Commission in United States) are more useful and highly recommended in our country. A statement (on p. 41) indicating that 115° C. in the autoclave for 15 minutes should not be exceeded, would not be accepted by many workers in the United States.

This volume is of interest to indicate the needs of students abroad and as a reference for those in the field of microbiology.

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